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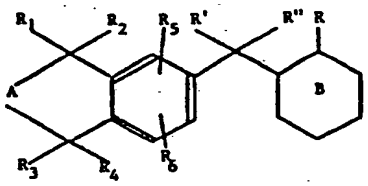
(54) New bicyclic aromatic derivatives, and use thereof in cosmetics and in human and veterinary medicine

(57) A compound of formula:



(I)

in which:

R_1, R_2, R_3 and R_4 each represent hydrogen or lower alkyl, with the proviso that at least two of R_1 to R_4 are other than hydrogen;

A represents methylene or dimethylene which may optionally be substituted by lower alkyl with the further possibility that when A represents dimethylene, R_1 and R_3 may together form a methylene or dimethylene radical;

R_5 and R_6 each represents hydrogen, halogen, lower alkyl, lower alkoxy, or hydroxyl;

R' represents hydrogen, hydroxyl, lower alkoxy, C_1–C_4 acyloxy or an amino radical;

R" represents hydrogen or lower alkoxy, or R' and R" may together form an oxo (=O), methano ($=CH_2$) or hydroxyimino (=N–OH) radical;

B represents a cyclohexyl, cyclohexenyl, cyclohexadienyl or phenyl ring which may be substituted or unsubstituted; and

R represents $-CH_2OH$ or a $-COR_7$ radical, in which R_7 is hydrogen, or an $-OR_8$ radical, or an amino radical.

Compounds I may be used for the treatment of skin having a greasy appearance; additionally they have an activity in the local and systemic treatment of skin disorders with an inflammatory component.

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SPECIFICATION

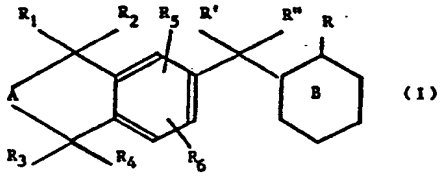
New bicyclic aromatic derivatives, process for the preparation thereof and use thereof in cosmetics and in human and veterinary medicine

The present invention relates to new bicyclic aromatic compounds, to the process for the preparation thereof and to the use thereof in cosmetics and in human and veterinary medicine.

Because of their inhibiting activity towards lipid synthesis, the compounds according to the invention are of great interest in cosmetics for the treatment of scalp and of skin having a greasy appearance.

Additionally, these compounds have an activity in the local and systemic treatment of skin disorders with an inflammatory component.

The bicyclic aromatic compounds according to the invention may be represented by the following general formula:



(I)

in which:

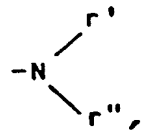
R_1, R_2, R_3 and R_4 represent, independently from one another, a hydrogen atom or a lower alkyl radical, at least two of the radicals R_1 to R_4 being other than a hydrogen atom,

A represents a methylene or dimethylene radical substituted by a lower alkyl radical or unsubstituted; when A represents a dimethylene radical, R_1 and R_3 may together form a methylene or dimethylene radical, R_5 and R_6 represent a hydrogen atom, a halogen atom, a lower alkyl radical, a lower alkoxy radical or a hydroxyl radical, R' represents a hydrogen atom, a hydroxyl radical, a lower alkoxy radical, a C_1–C_4 acyloxy radical or an amino radical,

R" represents a hydrogen atom or a lower alkoxy radical, or R' and R" taken together, form an oxo (=O), methano ($=CH_2$) or hydroxyimino (=N–OH) radical,

B represents a cyclohexyl, cyclohexenyl, cyclohexadienyl or phenyl ring which may be substituted or unsubstituted,

R represents $-CH_2OH$ or the radical $-COR_7$, R_7 being a hydrogen atom, or the radical $-OR_8$ of



R_8 representing a hydrogen atom, an alkyl radical containing from 1 to 20 carbon atoms, an optionally substituted monohydroxyalkyl, polyhydroxylalkyl, aryl or aralkyl radical or a sugar residue,

r' and r" representing a hydrogen atom, a lower alkyl radical, a monohydroxyalkyl radical optionally interrupted by a hetero atom, a polyhydroxyalkyl radical, an optionally substituted aryl or benzyl radical, an amino acid or amino sugar residue or, taken together, form a heterocycle,

and the salts of the said compounds of formula (I) and their optical isomers as well as the tautomeric forms of the compounds of formula (I), with the exception of 2-[(5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid.

By lower alkyl radical must be understood a radical containing from 1 to 6 carbon atoms.

By lower alkyl radical or alkyl radical containing up to 20 carbon atoms must be understood especially methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, 2-ethylhexyl, octyl, dodecyl, hexadecyl and octadecyl radicals.

By monohydroxy radical must be understood a radical containing from 2 to 6 carbon atoms, especially a 2-hydroxyethyl, 2-hydroxypropyl or 2-hydroxyethoxyethyl radical.

By polyhydroxyalkyl radical must be understood–a radical containing from 3 to 6 carbon atoms and from 2 to 5 hydroxyl groups, such as 2,3-dihydroxypropyl and 1,3-dihydroxy-2-propyl radicals or pentaerythritol residue.

Among lower alkoxy radicals, there may be mentioned, in particular, methoxy, isopropoxy, butoxy and tert-butoxy radicals.

By a sugar residue must be understood a residue derived for example from glucose, mannose, erythrose or galactose.

Among amino sugar residues, there may be mentioned those derived from glucosamine,

galactosamine, mannosamine or meglumine.

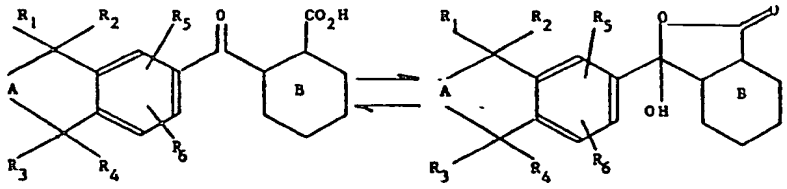
When radical B is a substituted phenyl ring, the substituents may be a lower alkyl, a halogen or an alkoxy in position 3, 4, 5 or 6.

When radical r' and r'' taken together form, with the nitrogen atom to which they are attached, a heterocycle, the latter is preferably a piperidino, piperazino, morpholino, pyrrolidino or 4-(2-hydroxyethyl)piperazino radical.

When the compounds according to the invention are in the form of salts, these may be *either* salts of zinc, of an alkali metal or alkaline earth metal or of an organic amine when they contain at least one free acid group, *or* salts of an inorganic or organic acid, especially hydrochloride, hydrobromide or citrate when they contain at least one amine group.

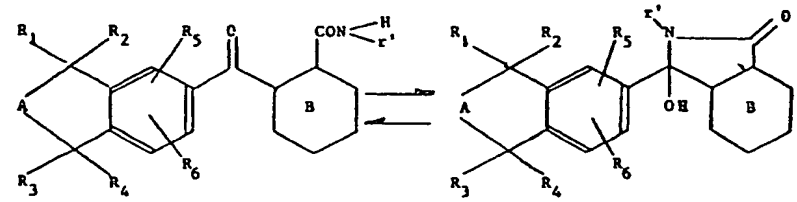
The compounds according to the invention may be in the tautomeric form when R' and R'' taken together form an oxo radical and R represents a carboxylic acid group or an amide group.

Thus, the compounds of formula (II) above may be in the lactone cyclic form (III).



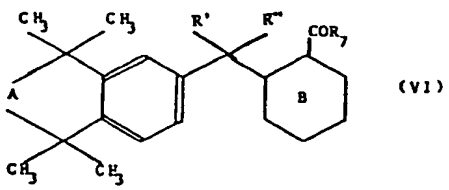
(II) (III)

Similarly, compounds of formula (IV) may be in the lactam tautomeric form of formula (V).



(IV) (V)

Among the particularly preferred compounds of formula (I) according to the invention, there may be mentioned, in particular, those corresponding to the following general formula:



(VI)

in which:

R' and R'' taken together form an oxo radical (=O) or R' represents a hydroxyl radical and R'' a hydrogen atom,

A represents a radical $-(CH_2)_2$ or the radical $-\underset{\underset{CH_3}{|}}{CH}-$

B is a phenyl or cyclohexyl ring,

R_7 represents the radical OR_8 or the radial $-N\begin{matrix}r'\\ \diagdown\\ \diagup\\ r''\end{matrix}$

R_8 representing a hydrogen atom or an alkyl radical containing from 1 to 12 carbon atoms,

r' representing a hydrogen atom or a monohydroxyalkyl radical,

r'' representing an alkyl radical containing from 1 to 8 carbon atoms, a monohydroxyalkyl

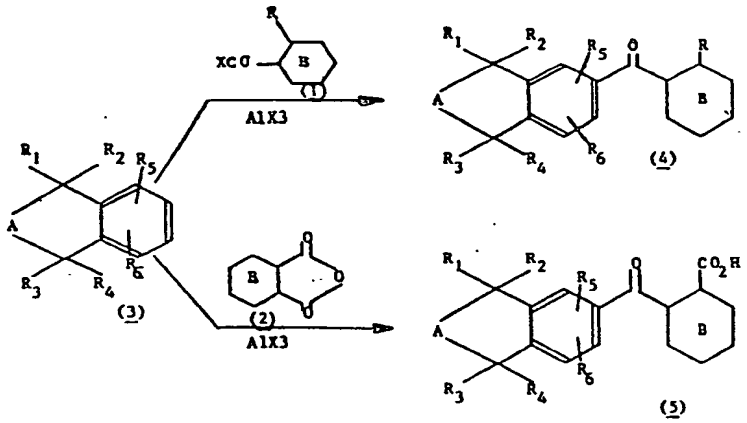
radical optionally interrupted by a hetero atom, or a polyhydroxyalkyl radical or r' and r'', taken together, form with the nitrogen atom, a 4-(2-hydroxyethyl)piperazinyl radical and the salts of the said compounds of formula (VI).

Among the compounds of formula (I) according to the invention, the following may be mentioned in particular:

(1) 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid,
(2) N-Ethyl-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(3) Methyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(4) 2'-Ethylhexyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(5) Sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(6) Zinc 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(7) 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzaldehyde,
(8) 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]phenylcarbinol,
(9) 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzoic acid,
(10) N-4'-(2-Hydroxyethyl)piperazino-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(11) 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)ethoxymethyl]benzoic acid,
(12) 2-[(1,1,2,3,3-Pentamethyl-5-indanyl)hydroxymethyl]benzoic acid,
(13) 2-[2-(1,1,2,3,3-Pentamethyl-5-indanyl)-2-ethenyl]benzoic acid,
(14) 2-[(1,1,2,3,3,-Pentamethyl-5-indanyl)carbonyl]benzoic acid,
(15) N-Ethyl-2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzamide,
(16) Ethyl 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]-benzoate,
(17) 2'-Ethylhexyl 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoate,
(18) Sodium 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoate,
(19) N-4'-(2-Hydroxyethyl)piperazino 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzamide,
(20) 2-(1,1,3,3-Tetramethyl-5-indanyl)hydroxymethyl]benzoic acid,
(21) 2-[(1,1,3,3-Tetramethyl-5-indanyl)carbonyl]benzoic acid,
(22) N-Ethyl-2-[(1,1,3,3-tetramethyl-5-indanyl)carbonyl]benzamide,
(23) N-4'-(2-Hydroxyethyl)piperazino-2-[(1,1,3,3-tetramethyl-5-indanyl)carbonyl]benzoamide,
(24) Zinc 2-[(1,1,3,3-tetramethyl-5-indanyl)carbonyl]benzoate,
(25) Ethyl 2-[(5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(26) N-Ethyl-2-[(5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(27) 2-[(5,8-Methano-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzoic acid,
(28) 2-[(1,4-Dimethoxy-5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzoic acid,
(29) 2-[(1,4-Dimethoxy-5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid,
(30) N-Ethyl-2-[(1,4-dimethoxy-5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(31) N,N-Di-n-butyl-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(32) 2-[5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid,
(33) 2-[(1,1,2,3,3-Pentamethyl-5-indanyl)carbonyl]-1-cyclohexene-1-carboxylic acid,
(34) N,N-Di(2-hydroxyethyl)-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(35) Sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate,
(36) 2-[(1,1,2,3,3-Pentamethyl-5-indanyl)carbonyl]cyclohexanecarboxylic acid,
(37) Ethyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate,
(38) 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylic acid,
(39) Sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylate,
(40) Ethyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(41) 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)methyl]benzoic acid,
(42) Zinc 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate and
(43) Zinc 2-[5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate.

The present invention also relates to the process for the preparation of bicyclic aromatic compounds of formula (I).

These compounds may be prepared according to the reaction scheme below:



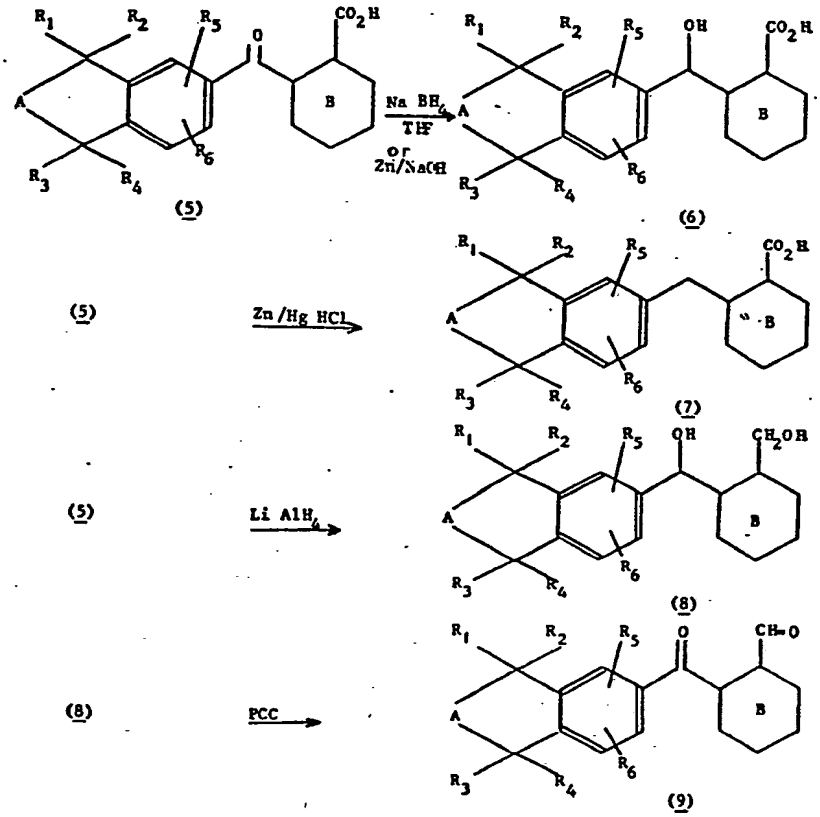
X=Cl or Br

In a first stage, these compounds result from a condensation under the conditions of the Friedel-Crafts reaction either of a substituted acid halide (*1*), or of an anhydride of structure (*2*) with a bicyclic aromatic compound of formula (*3*).

The condensation reaction is preferably carried out using an internal anhydride of structure (*2*) in the presence of a Lewis acid such as aluminium chloride or tin chloride in a chlorinated solvent such as 1,2-dichloroethane.

Among the starting bicyclic aromatic compounds of formula (*3*), there may be mentioned 1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene [described in J.A.C.S., *62*, 36–44, (1940)], 1,4-methano-1,2,3,4-tetrahydronaphthalene or benzonorbornene [described in J.O.C., *32*, 893–901, (1967)], 5,8-dihydroxy-1,4-methano-1,2,3,4-tetrahydronaphthalene (commercial product), 1,1,3,3-tetramethylindane and 1,1,2,3,3-pentamethylindane (described in French Patent 1,392,804).

Other forms of the compounds according to the invention may be prepared according to the following reaction scheme starting with compounds of formulae (*4*) and (*5*), especially starting with the keto acids of formula (*5*).



Thus, the secondary alcohols of formula (*6*) may be prepared by reduction using sodium borohydride, in a solvent such as tetrahydrofuran or alternatively, using zinc in an alkaline medium.

Compounds of formula (*7*) may be prepared by Clemmensen reduction using zinc amalgam in the presence of hydrochloric acid.

The diols of formula (*8*) may be prepared by reduction using lithium aluminium hydride in tetrahydrofuran.

The keto aldehydes of formula (*9*) may be obtained by oxidation using pyridinium chlorochromate (P.C.C.) starting with these diols.

The acyloxy derivatives of the compounds of formula (I), (R′=acyloxy and R″=H) are obtained by reacting an activated form of acid, such as an anhydride or an acid chloride, with a compound according to the invention in which R′=OH and R″=H.

Similarly, the alkoxy derivatives of the compounds of formula (I), (R′=alkoxy and R″=H) are obtained starting with compounds of formula (I) (R′=OH and R″=H) according to known methods.

The compounds of formula (I) in which R′ and R″ together form a methano radical (CH_2=) are obtained by the action of methyltriphenylphosphonium bromide, in a basic medium, on the carbonyl-containing compounds of formula (I) in which R′ and R″ taken together form an oxo radical.

The compounds of formula (I) in which R′ and R″ together form a hydroxyimino radical are obtained by reacting hydroxylamine hydrochloride with the corresponding carbonyl-containing compounds, in an organic solvent such as ethanol, in the presence of an inorganic base such as sodium bicarbonate or of an organic base such as triethylamine.

On reduction with zinc in an acetic acid medium, these hydroxyimino derivatives lead to the corresponding amines (R′=NH_2 and R″=H).

The compounds of formula (I), according to the present invention, show an excellent activity in the test described by J. GIRARD and A. BARBIER, Int. Journal of Cosmetic Science *2*, 315–329 (1980) and M. GAUCI and J. OUSTRIN, Int. Journal of Cosmetic Science *3*, 227–232 (1982). In fact, these authors have shown that the "in vitro" labelled glucose incorporation test could be adopted as a preliminary test for non-hormonal antiseborrhoeics because this test takes account of the inhibitory activity towards lipid synthesis.

However, it is known that an increase in sebum secretion produces skin conditions such as seborrhoea, dandruff, greasy skin, greasy hair, white spots and black spots. These chronic

phenomena of pilosebaceous units are especially related to the face, the chest and the back.

Additionally, the acids of formula (I) according to the invention in which R=$-CO_2H$ show a bactericidal activity against organisms causing acne.

Therefore, these compounds are particularly well suited for treating skin conditions related to a disorder involving an excessive production or secretion of sebum and for skin or other conditions with an inflammatory component, especially

acne vulgaris, comedonic or polymorphic acnes, senile acnes, acne solaris and acne medicamentosa or trade acne.

Therefore, the subject of the present invention is also a new medicinal composition, intended in particular for the treatment of the abovementioned conditions, characterized in that it contains at least one compound of formula (I) and/or one of its isomers, and/or one of its tautomeric forms, and/or one of its salts in a pharmaceutically acceptable vehicle.

As vehicle for the compositions, any conventional vehicle may be employed, the active compound being either in a dissolved state or in a dispersed state in the vehicle.

The administration may be carried out enterally, parenterally, locally or through the eye. For enteral administration, the medicaments may be in the form of tablets, gelatin capsules, dragees, syrups, suspensions, solutions, powders, granules or emulsions. For parenteral administration, the compositions may be in the form of solutions or suspensions for perfusions or for injections.

The compounds according to the invention are generally administered at a daily dose of approximately 0.1 mg/kg to 10 mg/kg of body weight.

For local application, the pharmaceutical compositions based on the compounds according to the invention are in the form of ointments, tinctures, creams, pomades, powders, patches, impregnated pads, solutions, emulsions, lotions, gels, sprays or suspensions.

These compositions for local application may be in an anhydrous form or in an aqueous form depending on the clinical indication.

When the compounds according to the invention are used by local application, a good activity of these compounds is observed over a very wide range of dilution; active substance concentrations ranging from 0.01 to 10% by weight may especially be used. It is, of course, possible to use higher concentrations when this becomes essential for a specific therapeutic application; however, the preferred active substance concentrations are between 0.1 and 5% by weight.

The compounds according to the invention also find an application in the cosmetic field, in particular body and hair hygiene and especially for the treatment of skins which tend to be affected by acne, for hair regrowth, anti-hair loss, for treatment against the greasy appearance of the skin and the hair, and in the prevention or treatment of harmful effects of sunlight.

Therefore, the present invention also relates to a cosmetic composition, containing at least one compound of formula (I) or one of its salts in a cosmetically acceptable vehicle, this composition especially being in the form of a lotion, a gel, a soap or a shampoo.

The concentration of the compound of formula (I) in the cosmetic compositions is between 0.005 and 5% by weight and preferably between 0.01 and 1% by weight.

The medicinal and cosmetic compositions according to the invention may contain inert or even pharmacodynamically or cosmetically active additives and especially: moisturising agents such as thiamorpholinone and its derivatives or urea; antisebhorrhoeic agents such as S-carboxymethylcystein, S-benzylcysteamine and their derivatives, and tioxolone; anti-acne agents such as benzoyl peroxide; antibiotics such as erythromycin and its esters, neomycin, tetracyclines or 4,5-polymethylene-3-isothiazolinones; agents promoting hair regrowth, such as "Minoxidil" (2,4-diamino-6-piperidinopyrimidine-3-oxide) and its derivatives, Diazoxide (7-chloro-3-methyl-1,2,4-benzothiadiazine-1,1-dioxide) and Phenytoin (5,5-diphenylimidazoline-2,4-dione) or oxapropanium iodide; stearoid or non-steroid antiinflammatory agents; carotenoids and especially β-carotene; and antipsoriatic agents such as anthralin and its derivatives and eicosa-5,8,11,14-tetraynoic and -5,8,11-triynoic acids, their esters and amides.

The compositions according to the invention may also contain flavour-improving agents, preservatives, stabilizers, moisture-regulating agents, pH-regulating agents, osmotic pressure-modifying agents, emulsifiers, UV–A and UV–B filters and antioxidants such as 1'd-tocopherol, butylhydroxyanisole or butylhydroxytoluene.

Several examples of preparation of the active compounds of formula (I) according to the invention and examples of compositions containing them will now be given by way of illustration, without being limiting in nature.

EXAMPLE I

Preparation of 2[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid

(Formula I in which A=$-(CH_2)_2$, $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo, B=phenyl; R=CO_2H)

13.3 g (0.1 mol) of anhydrous aluminium chloride are added, in portions, to a suspension of 9.41 g (0.05 mol) of 1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene and 7.46 g (0.05 mol) of

phthalic anhydride in 100 cm³ of anhydrous 1,2-dichloroethane so as to maintain the temperature below 30°C. After stirring for 1 hour at ambient temperature, the reaction medium is poured into 100 cm³ of ice-cold water. The organic phase is decanted. The aqueous phase is extracted again with 2 × 150 cm³ of dichloroethane. The dichloroethane phases are combined, washed with water, dried over sodium sulphate and then concentrated under reduced pressure. The crude solid obtained is taken up with 250 ml of boiling hexane, drained after cooling at +5°C and recrystallized in 200 cm³ of toluene. After drying under vacuum at 80°C, 13.5 g of white crystals of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid with a melting point of 187°C are obtained.

The 250 MHz ^1H NMR and the I.R. spectra are in agreement with the expected structure.

Elemental analysis: $C_{22}H_{24}O_3$

	C	H	O
calculated	78.54	7.19	14.27
found	78.82	6.93	14.25

EXAMPLE II

Preparation of 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoic acid
(Formula I in which A = –CH(CH₃)–; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=phenyl; R=CO_2H)

16 g (0.12 mol) of anhydrous aluminium chloride are added, in portions, to a suspension of 13.2 g (0.07 mol) of 1,1,2,3,3-pentamethylindane and 10.37 g (0.07 mol) of phthalic anhydride in 150 cm³ of anhydrous 1,2-dichloroethane so as to maintain the temperature below 30°C. After stirring for 1 h at ambient temperature, the reaction medium is poured into 100 cm³ of ice-cold water. The organic phase is decanted. The aqueous phase is extracted again with 2 × 100 cm³ of dichloroethane. The dichloroethane phases are combined, washed with water, dried over sodium sulphate and then concentrated under reduced pressure. The crude solid obtained is taken up with hexane, drained, and then recrystallized in ethyl acetate. After drying, 15.5 g of white crystals of 2-[1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoic acid with a melting point of 205°C are obtained.

The 80 MHz ^1H NMR and the I.R. spectra correspond to the expected structure.

Elemental analysis: $C_{22}H_{24}O_3$

	C	H	O
calculated	78.54	7.19	14.27
found	78.50	7.20	14.15

EXAMPLE III

Preparation of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid
(Formula I in which A = –$(CH_2)_2$–; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=cyclohexyl; R=CO_2H)

20 g (0.15 mol) of anhydrous aluminium chloride are added, in portions, to a suspension of 16.95 g (0.09 mol) of 1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene and 13.9 g (0.09 mol) of cis-hexahydrophthalic anhydride in 150 cm³ of anhydrous 1,2-dichloroethane so as to maintain the temperature below 30°C. After stirring for 1 h at ambient temperature, the reaction medium is poured into 100 cm³ of ice-cold water. The organic phase is decanted. The aqueous phase is extracted again with 150 cm³ of dichloroethane. The dichloroethane phases are combined, washed with water, dried over sodium sulphate and then concentrated under reduced pressure. The crude solid obtained is taken up with lukewarm hexane, drained and then recrystallized in ethyl acetate. After drying, 20.7 g of white crystals of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid with a melting point of 173°C are obtained.

The 80 MHz ^1H NMR and the I.R. spectra are in agreement with the expected structure.

Elemental analysis: $C_{22}H_{30}O_3$

	C	H	O
calculated	77.15	8.83	14.02
found	76.93	8.89	13.97

EXAMPLE IV

Preparation of 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]-1-cyclohexene-1-carboxylic acid

(Formula I in which A=$-\underset{\displaystyle CH_3}{\overset{|}{CH}}-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=cyclohexenyl; $R=CO_2H$)

8.3 g (0.06 mol) of anhydrous aluminium chloride are added, in portions, to a suspension of 5.88 g (0.031 mol) of 1,1,2,3,3-pentamethylindane and 5 g (0.031 mol) of 3,4,5,6-tetrahydrophthalic anhydride in 60 cm³ of anhydrous 1,2-dichloroethane so as to maintain the temperature below 30°C. After stirring for 2 h, the reaction medium is poured into 40 cm³ of ice-cold water. The organic phase is decanted. The aqueous phase is extracted again with 2 × 150 cm³ of dichloroethane. The dichloroethane phases are combined, washed with water, dried over sodium sulphate and then concentrated under reduced pressure. The crude solid obtained is purified by chromatography on silica gel 60, eluted with dichloromethane and crystallized in hexane. After filtering and drying, 4.8 g of white crystals of 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]-1-cyclohexene-1-carboxylic acid with a melting point of 153°C are obtained.

The 250 MHz ^1H and ^{13}C NMR specta in deuterochloroform and the I.R. spectra (KBr and dichloromethane) correspond to the lactone cyclized form.

Elemental analysis: $C_{22}H_{28}O_3$

	C	H	O
calculated	77.61	8.29	14.10
found	77.94	8.47	13.53

EXAMPLE V

Preparation of 2-[(1,4-dimethoxy-5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid

(Formula I in which A=$-(CH_2-)_2-$; R_1 and $R_3=-CH_2-$; $R_2=R_4=H$; $R_5=R_6=-OCH_3$; R', R''=OXO; B-phenyl; $R=-CO_2H$)

2.93 g (22 mmol) of anhydrous aluminium chloride are added, in portions, in the course of approximately 30 min, to a suspension of 2.25 g (11 mmol) of 5,8-dimethoxy-1,4-methano-1,2,3,4-tetrahydronaphthalene and 1.63 g (11 mmol) of phthalic anhydride in 40 ml of anhydrous 1,2-dichloroethane. After stirring overnight at ambient temperature, the reaction medium is poured into 40 cm³ of ice-cold water. The organic phase is decanted. The aqueous phase is extracted again with 2 × 100 cm³ of dichloromethane. The dichloroethane and dichloromethane phases are combined, washed with water, dried over sodium sulphate and evaporated to dryness. The solid obtained is purified twice by chromatography on silica gel 60, eluting with a dichloromethane:tetrahydrofuran 50:50 mix-ture. After evaporating and drying, the solid isolated is taken up with isopropyl ether. After filtering and drying, 0.4 g of 2-[(1,4-dimethoxy-5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid with a melting point of 213°C is obtained in the form of a white powder.

The 80 MHz ^1H NMR spectrum is in agreement with the expected structure.

Elemental analysis: $C_{21}H_{20}O_5$

	C	H	O
calculated	71.38	5.72	22.70
found	71.18	5.76	22.67

EXAMPLE VI

Preparation of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]phenylcarbinol.

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$, R'=OH; R''=H; B=phenyl; $R=CH_2OH$)

A solution of 1 g (3 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]-benzoic acid in 20 cm³ of anhydrous tetrahydrofuran is added dropwise to a suspension of 350 mg (9 mmol) of lithium aluminium hydride in 10 cm³ of anhydrous tetrahydrofuran, cooled to 0°C. After stirring for 1 h and allowing to return to ambient temperature, the reaction medium is cooled to 0°C, acidified by adding slowly 0.1 N hydrochloric acid and extracted with ethyl ether. The organic phase is washed with water, dried over sodium sulphate and evaporated to dryness. The crude diol obtained is purified by chromatography on silica gel 60, eluted with a dichloromethane: ethyl acetate 97:3 mixture. After evaporating, a colourless oil is obtained, which is crystallised in hexane. After filtering and drying, 0.8 g of white crystals of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]phenylcarbinol with a melting point of 95–98°C are obtained.

The 80 MHz ^1H NMR spectrum corresponds to the expected structure.

Elemental analysis: $C_{22}H_{28}O_2$

	C	H	O
calculated	81.44	8.70	9.86
found	81.48	8.46	9.82

EXAMPLE VII

Preparation of 2'-ethylhexyl 2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6$;H; R',R''=oxo; B=phenyl; R=$-CO_2C_8H_{17}$)

A solution of 4.2 g (0.0125 mol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid described in Example I and 3.26 g (0.025 mol) of 2-ethyl-1-hexanol in 100 cm³ of toluene containing 0.1 cm³ of 98% sulphuric acid is heated under reflux for 8 h, the water formed being distilled azeotropically. The reaction medium is then cooled to ambient temperature, thoroughly washed with water and concentrated under reduced pressure. The crude oil obtained is quickly purified by chromatography on silica gel 60, eluted with a toluene:dichloromethane 50:50 mixture. After evaporating and drying, 4.1 g of 2'-ethylhexyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate are obtained in the form of a colourless liquid.

The 80 MHz ^{1}NMR and the I.R. spectra correspond to the expected structure.

Elemental analysis: $C_{30}H_{40}O_3$

	C	H	O
calculated	80.31	8.99	10.70
found	80.46	8.91	10.75

EXAMPLE VIII

Preparation of ethyl 2-[(1,1,2,3,3,-pentamethyl-5-indanyl)carbonyl]benzoate

(Formula I in which A=$-\underset{\displaystyle CH_3}{\overset{|}{CH}}-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6$=H; R',R''=oxo; B=phenyl; R=$CO_2C_2H_5$)

A solution of 2.4 g (7.1 mmol) of 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoic acid described in Example II, in 80 cm³ of ethyl alcohol containing 0.1 cm³ of 98% sulphuric acid is heated under reflux for 12 h. The solution is then concentrated under reduced pressure. The crude ester is dissolved in 100 cm³ of ethyl ether. The ethereal solution is washed with sodium bicarbonate and then with water, dried over sodium sulphate and finally evaporated to dryness. After drying, 2.5 g of ethyl 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoate are obtained in the form of a colourless oil which crystallizes slowly at ambient temperature to give a white solid with a melting point of 56–57°C.

The 80 MHz ^1H NMR and the I.R. spectra are in agreement with the expected structure.

Elemental analysis: $C_{24}H_{28}O_3$

	C	H	O
calculated	79.09	7.74	13.17
found	79.12	7.85	12.98

EXAMPLE IX

Preparation of methyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate

(Formula I in which A=$-(CH_2)_2$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6$=H; R', R''=oxo, B=phenyl; R=$-CO_2CH_3$)

A solution of 3.36 g (0.01 mol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid described in Example I, in 125 cm³ of methyl alcohol containing 0.1 cm³ of 98% sulphuric acid is heated under reflux for 24 h. The solution is concentrated under reduced pressure. The crude ester is dissolved in 150 cm³ of ethyl ether, washed with sodium bicarbonate and with water. After drying over sodium sulphate, the ethereal phase is evaporated to dryness. The solid obtained is recrystallized in a minimum quantity of hexane. After drying, 2.2 g of white crystals of methyl 2-[(5,5-8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]ben-

zoate with a melting point of 77–78°C are obtained.

The 80 MHz ^1H NMR and the I.R. spectra correspond to the expected structure.

Elemental analysis: $C_{23}H_{26}O_3$

	C	H	O
calculated	78.82	7.48	13.70
found	78.93	7.50	13.79

EXAMPLE X

Preparation of N-ethyl-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=phenyl; R=$-CONHC_2H_5$)

0.55 cm³ (6 mmol) of phosphorus trichloride is added to a solution of 3.36 g (0.01 mol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid in 30 cm³ of anhydrous dichloromethane and the mixture is heated under reflux for 3 h. The reaction medium is then cooled to +5°C and 2 cm³ (0.03 mol) of anhydrous ethylamine are added. The stirring is maintained for 30 min at +5°C and then for 1 h allowing the mixture to return to ambient temperature. The reaction medium is then diluted to 100 cm³ by adding dichloromethane and washed with dilute hydrochloric acid and then with water. The dichloromethane phase is dried over sodium sulphate and then concentrated under reduced pressure. The crude product obtained is purified by chromatography on silica gel 60, eluting with a toluene:dichloromethane:ethyl acetate 5:3:2 mixture, followed by a recrystallization in isopropyl ether. After drying, 1.75 g of white crystals of N-ethyl-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide with a melting point of 201°C are obtained.

The 250 MHz ^1H and ^{13}C NMR spectra in deuterochloroform and the I.R. spectra (KBr and dichloromethane) correspond to the lactam cyclized form.

Elemental analysis: $C_{24}H_{29}NO_2$

	C	H	N	O
calculated	79.30	8.04	3.85	8.80
found	79.32	8.01	3.80	8.69

EXAMPLE XI

Preparation of N,N-di-n-butyl-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo, B=phenyl; R=$-CON(C_4H_9)_2$

0.22 cm³ (2.5 mmol) of phosphorus trichloride is added to a solution of 1.68 g (5 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid in 20 cm³ of anhydrous dichloromethane and the mixture is heated under reflux for 3 h. After cooling to +5°C, 2.6 cm³ (15 mmol) of dibutylamine are added. Stirring is maintained for 30 min at +5°C and then for an additional period of 1 h allowing the mixture to return to ambient temperature. The reaction medium is then diluted to approximately 80 cm³ by adding dichloromethane and then transferred into a separating funnel and washed with dilute hydrochloric acid and then with water. The dichloromethane phase is dried over sodium sulphate and then concentrated under reduced pressure. The crude product obtained is purified by chromatography on silica gel 60, eluting with a toluene:dichloromethane:ethyl acetate 5:3:2 mixture. After evaporating and drying under vacuum at 80°C, 0.6 g of N,N-di-n-butyl-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide is obtained in the form of a colourless thick oil.

The 80 MHz ^1H NMR and the I.R. spectra correspond to the expected structure.

Elemental analysis: $C_{30}H_{41}NO_2$; 0.25 H_2O

	C	H	N	O
calculated	79.69	9.25	3.10	7.96
found	79.48	9.37	3.16	7.97

EXAMPLE XII

Preparation of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzaldehyde

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=phenyl;

R=–CHO)

2.3 g (10.6 mmol) of pyridinium chlorochromate are added to a solution of 1 g (3 mmol) of 2[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]phenylcarbinol described in Example VI, in 20 cm^3 of dry dichloromethane, which is stirred at ambient temperature and the mixture is stirred for 1 h 30 min at a temperature less than or equal to 28°C. After diluting to approximately 200 cm^3 with dichloromethane, 50 g of silica gel 60 are added and the mixture is filtered through celite. The filtrate is concentrated under reduced pressure. The crude solid obtained is purified by chromatography on silica gel 60, eluted with dichloromethane. After evaporating and drying under vacuum at 70°C, 0.3 g of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzaldehyde is obtained in the form of a white solid with a melting point of 145°C.

The 80 MHz ^1H NMR spectrum is in agreement with the expected structure.

Elemental analysis: $C_{22}H_{24}NO_2$

	C	H	O
calculated	82.46	7.55	9.99
found	82.88	7.37	9.82

EXAMPLE XIII

Preparation of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzoic acid and its lactone

(Formula I in which A=–$(CH_2–)_2$–; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R'=OH, R''=H; B=phenyl; R=CO_2H)

1.82 cm^3 (0.048 mmol) of sodium borohydride are added, in portions, to a solution of 2 g (8.12 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid in 50 cm^3 of anhydrous tetrahydrofuran and the mixture is stirred for 20 h at ambient temperature. The reaction medium is cooled to between 0 and 5°C, acidified by adding slowly 0.1 N hydrochloric acid and extracted with ethyl ether. The organic phase is washed with water, dried over sodium sulphate and evaporated to dryness. The crude product obtained is quickly purified by chromatography on silica gel 60, eluting with dichloromethane, followed by a recrystallization in hexane. After drying, 1.1 g of white crystals of the lactone of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzoic acid with a melting point of 134°C are obtained.

The 250 MHz ^1H and ^{13}C NMR spectra and the I.R. spectra correspond to the expected structure.

Elemental analysis: $C_{22}H_{24}NO_2$

	C	H	O
calculated	82.46	7.55	9.99
found	82.45	7.60	10.11

A suspension of 0.96 g (3. mmol) of the lactone described above in 60 cm^3 of normal sodium hydroxide is heated under reflux for 2 h. The solution obtained is cooled to +5°C and then acidified by adding 3.5 cm^3 of glacial acetic acid. The precipitate obtained is filtered, thoroughly washed with water and dried under vacuum over potassium hydroxide at ambient temperature. 0.96 g of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzoic acid in the form of a well crystallized and very hydrophobic white solid which becomes gummy as soon as it is heated and then becomes solid again and melts at 134°C (conversion into lactone).

The 250 MHz ^1H NMR and the I.R. spectra are in agreement with the expected structure.

Elemental analysis: $C_{22}H_{26}NO_3$

	C	H	O
calculated	78.07	7.74	14.18
found	77.97	7.72	13.89

EXAMPLE XIV

Preparation of sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate

(Formula I in which A=–$(CH_2–)_2$–; $R_1=R_2=R_3=R_4=CH_3$– $R_5=R_6=H$; R',R''=oxo; B=phenyl; R=$CO_2^{\ominus}Na^{\oplus}$)

1.252 g (3.73 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid are suspended in 300 cm^3 of double-deionized water, 37.3 cm^3 of 0.1 N aqueous sodium

hydroxide (3.73 mmol) are added and the mixture is stirred, warming until the contents are dissolved. The solution is filtered and then evaporated to dryness. 50 cm³ of toluene are then added and the solution is again evaporated to dryness. After drying under vacuum at 80°C, 1.32 g of sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate are thus obtained in the form of a white powder with a melting point higher than 300°C.

EXAMPLE XV

Preparation of sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate

(Formula I in which A=$-(CH_2)_2$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=cyclohexyl; R=$-CO_2^{\ominus}Na^{\oplus}$)

342.5 mg (1 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid are suspended in 150 cm³ of double-deionized water, 10 cm³ of 0.1 N sodium hydroxide (1 mmol) are added and the mixture is stirred, warming until the contents are dissolved. The solution obtained is then filtered and then evaporated to dryness. 50 cm³ of toluene are added and the solution is again evaporated to dryness. After drying under vacuum at 80°C, 0.36 g of sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate is thus obtained in the form of a white solid which becomes glassy between 145 and 150°C.

EXAMPLE XVI

Preparation of 2-[(1,1,3,3-tetramethyl-5-indanyl)carbonyl]benzoic acid

(Formula I in which A=$-CH_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R', R''=oxo; B=phenyl; R=$-CO_2H$)

3.4 g (25.5 mmol) of anhydrous aluminium chloride are added, in portions, to a suspension of 2.96 g (17 mmol) of 1,1,3,3-tetramethylindane and 2.52 g (17 mmol) of phthalic anhydride in 100 cm³ of anhydrous 1,2-dichloroethane so as to maintain the temperature below 30°C.

After stirring for 3 hours, the reaction medium is poured into 50 cm³ of ice-cold water. The organic phase is decanted. The aqueous phase is extracted again with 2×50 cm³ of dichloroethane. The dichloroethane phases are combined, washed with water, dried over sodium sulphate and then concentrated under reduced pressure. The residue is taken up with 100 cm³ of lukewarm hexane, drained after cooling to +5°C, washed with 2×50 cm³ of hexane and then recrystallized in a minimum volume of boiling toluene. After drying under vacuum at 80°C, 3.1 g of white crystals of 2-[(1,1,3,3-tetramethyl-5-indanyl)carbonyl]benzoic acid with a melting point of 194–195°C are obtained.

The 80 MHz ^1H NMR are the I.R. spectra are in agreement with the expected structure.

Elemental analysis: $C_{21}H_{22}O_3$

	C	H	O
calculated	75.49	7.75	16.76
found	75.47	7.67	16.92

EXAMPLE XVII

Preparation of 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]cyclohexanecarboxylic acid

(Formula I in which A=$-\underset{\underset{CH_3}{|}}{CH}-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=cyclohexyl; R=$-CO_2H$)

4.7 g (35 mmol) of anhydrous aluminium chloride are added, in portions, to a suspension of 3.3 g (17.5 mmol) of 1,1,2,3,3-pentamethylindane and 2.7 g (17.5 mmol) of cis-hexahydrophthalic anhydride in 100 cm³ of anhydrous 1,2-dichloroethane so as to maintain the temperature below 30°C. After stirring for 3 hours at ambient temperature, the reaction mixture is poured in 50 cm³ of ice-cold water. The organic phase is decanted. The aqueous phase is extracted again with 2×100 cm³ of dichloroethane. The dichloroethane phases are combined, washed with water, dried over sodium sulphate and then evaporated to dryness. The residue is taken up with 200 cm³ of lukewarm hexane, filtered after cooling to +5°C, washed with 3×100 cm³ of hexane, cooled and dried under vacuum at 70°C. 5.1 g of 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]cyclohexanecarboxylic acid is thus obtained in the form of a white solid with a melting point of 178°C.

The I.R. and the 80 MHz ^1H NMR spectra are in agreement with the expected structure.

Elemental analysis:	$C_{22}H_{30}O_3$		
	C	H	O
calculated	77.15	8.83	14.02
found	77.21	9.00	13.56

EXAMPLE XVIII

Preparation of N,N-di-(2-(hydroxyethyl)-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide

(Formula I in which: A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R,R''=oxo, B=phenyl; R=$-CON(CH_2CH_2OH)_2$)

0.44 cm³ of phosphorus trichloride is added to a solution of 3.36 g (10 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid described in Example I, in 30 cm³ of anhydrous dichloromethane and the mixture is heated under reflux for 3 hours. After cooling to +5°C, 5.25 g (0.05 mol) of diethanolamine are added and the mixture is stirred for 30 minutes at +5°C and then for 1 hour allowing the mixture to return to ambient temperature. The reaction medium is then diluted to approximately 80 cm³ and then transferred into a separating funnel and washed with dilute hydrochloric acid and then with water. The dichloromethane phase is dried over sodium sulphate and then concentrated under reduced pressure. The solid obtained is purified by chromatography on silica gel 60, eluting with an ethyl acetate:isopropyl alcohol: dichloromethane 3:2:5 mixture. After evaporating and drying, 3.2 g of N,N-di-(2-hydroxyethyl)-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide are obtained in the form of a white solid with a melting point of 116°C.

The 250 MHz ^1H NMR spectrum is in agreement with the expected structue.

Elemental analysis:	$C_{26}H_{33}NO_4$			
	C	H	N	O
calculated	73.73	7.85	3.31	19.11
found	73.51	7.88	3.27	19.40

EXAMPLE XIX

N-4'-(2-Hydroxyethyl)piperazino-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=phenyl; R=$-CONN-CH_2CH_2OH$

A solution of 1.68 g (5 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid described in Example I and 0.28 cm³ (3 mmol) of phosphorus trichloride in 15 cm³ of anhydrous dichloromethane is heated under reflux for 3 hours. After cooling to between 0 and +5°C, 1.4 cm³ (11.4 mmol) of N-(2-hydroxyethyl)piperazine are added and the mixture is stirred for 1 hour under light-proof conditions allowing it to return to ambient temperature. The reaction medium is then diluted to approximately 80 cm³ by adding dichloromethane and then transferred into a separating funnel and thoroughly washed with water. The dichloromethane phase is then dried over sodium sulphate and then concentrated under reduced pressure. The crude solid obtained is purified by chromatography on silica gel 60 under light-proof conditions, eluting first with a tetrahydrofuran:dichloromethane 50:50 mixture and then with tetrahydrofuran alone. After evaporating and drying under light-proof conditions, 0.9 of N-4'-(2-hydroxyethyl)piperazino-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide is obtained in the form of a white solid with a melting point of 58–60°C.

The 250 MHz ^1H NMR spectrum corresponds to the expected structure.

EXAMPLE XX

Preparation of ethyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=cyclohexyl; R=$-CO_2C_2H_5$)

A solution of 3.42 g (10 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid described in Example III, in 100 cm³ of ethyl alcohol containing 0.1 cm³ of 98% sulphuric acid is heated under reflux for 12 hours. The solution is concentrated under reduced pressure and the crude ester obtained is dissolved in 100 cm³ of ethyl ether. The

ethereal solution is washed with sodium bicarbonate and then with water, dried over sodium sulphate and evaporated to dryness. After drying, 3.6 g of ethyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate are obtained in the form of a colourless thick oil.

The I.R. and the 80 MHz ^1H NMR spectra correspond to the expected structure.

Elemental analysis: $C_{24}H_{34}O_3$

	C	H	O
calculated	77.80	9.25	12.95
found	77.65	9.29	12.78

EXAMPLE XXI

Preparation of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylic acid

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R'=OH, R''=H; B=cyclohexyl; R=$-CO_2H$)

A suspension of 3.42 g (10 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid described in Example III and 10 g of powdered zinc (0.15 mol) in 150 cm³ of an aqueous 2.5 M sodium hydroxide solution is heated under reflux for 7 hours. After cooling to +5°C, the reaction medium is neutralized with 60 cm³ of 6 N hydrochloric acid and then acidified to a pH in the region of 3 by adding 20 cm³ of glacial acetic acid. The mixture is then extracted with ethyl ether (2 × 150 cm³). The ethereal phase is thoroughly washed with water, dried over sodium sulphate and evaporated to dryness. The solid obtained is taken up with 50 cm³ of hexane, drained, washed again with 2 × 40 cm³ of hexane and dried under vacuum at 40°C. 2.9 g of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylic acid are thus obtained in the form of a white solid with a melting point of 186°C. The I.R. and the 250 MHz ^1H NMR spectra are in agreement with the expected structure.

Elemental analysis: $C_{22}H_{32}O_3$

	C	H	O
calculated	76.70	9.36	13.93
found	76.66	9.26	13.95

EXAMPLE XXII

Preparation of sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylate

(Formula I in which: A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R'=OH, R''=H; B=cyclohexyl; R=$CO_2^{\ominus}NA^{\oplus}$)

344.48 mg (1 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylic acid described in Example XXI are suspended in 100 cm³ of double-deionized water, 10 cm³ of 0.1 N aqueous sodium hydroxide (1 mmol) are added and the mixture is stirred for 30 minutes in an ultrasonic bath. The solution obtained is evaporated to dryness under reduced pressure. 50 cm³ of anhydrous toluene are added and the solution is again evaporated to dryness. After drying under vacuum at 80°C, 0.36 g of sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylate is thus obtained in the form of a white solid with a melting point of 260°C.

EXAMPLE XXIII

Preparation of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)methyl]benzoic acid

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R'=R''=H; B=phenyl; R=$-CO_2H$)

A mixture of 6 g of zinc, 0.6 g of mercuric chloride, 9 cm³ of water and 0.3 cm³ of concentrated hydrochloric acid is stirred for 10 min at ambient temperature. The solution is decanted and the amalgam is rinsed with 2 × 25 cm³ of water. 10 cm³ of water, 5 cm³ of concentrated hydrochloric acid, 8 cm³ of toluene, 8.4 g (0.025 mol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid described in Example I are then added and the mixture is heated under reflux for 30 hours, with stirring, adding 3 cm³ of concentrated hydrochloric acid every 6 hours. 20 cm³ of toluene are added, the mixture is filtered in the

heated state and the amalgam is washed with 3×40 cm³ of toluene. The filtrate is transferred into a separating funnel and the toluene phase is separated, washed with water, dried over sodium sulphate and then concentrated under reduced pressure. The crude product isolated is recrystallized in a heptane-isopropyl ether mixture. After drying, 6.6 g of white crystals of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)methyl]benzoic acid with a melting point of 136°C are obtained.

The 80 MHz ^{1}H NMR spectrum is in agreement with the expected structure.

Elemental analysis: $C_{22}H_{26}O_2$

	C	H	O
calculated	81.95	8.13	9.92
found	82.14	8.16	9.79

EXAMPLE XXIV

Preparation of ethyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=phenyl; R=$-CO_2C_2H_5$)

A solution of 8.41 g (0.025 mol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid described in Example I, in 300 cm³ of ethyl alcohol containing 0.4 cm³ of 98% sulphuric acid is heated under reflux for 14 hours. The solution is then concentrated under reduced pressure and the crude ester obtained is dissolved in 300 cm³ of ethyl ether. The ethereal solution is washed with sodium bicarbonate and then with water, dried over sodium sulphate and evaporated to dryness. After drying, 7.9 g of ethyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate are obtained in the form of a colourless oil which crystallizes slowly at ambient temperature to give a white solid with a melting point of 58–59°C.

The I.R. and the 80 MHz ^{1}H NMR spectra are in agreement with the expected structure.

Elemental analysis: $C_{24}H_{28}O_3$

	C	H	O
calculated	79.09	7.74	13.17
found	79.19	7.75	13.02

EXAMPLE XXV

Preparation of zinc 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=phenyl; R=$-CO_2^{\ominus}1/2Zn^{\oplus}$)

368.5 mg (1.1 mmol) of 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid described in Example I are suspended in 150 cm³ of double-deionized water, 11 cm³ (1.1 mmol) of 0.1 N sodium hydroxide are added and the mixture is stirred in an ultrasonic bath until the contents are dissolved (30 min). 157.5 mg (0.548 mmol) of zinc sulphate $7H_2O$ are added to the sodium salt solution thus obtained and the zinc salt formed by transalification precipitates. It is drained, washed with water and dried under vacuum at 70–80°C. 0.4 g of zinc 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate is thus obtained in the form of a white solid which becomes glassy at approximately 155°C.

EXAMPLE XXVI

Preparation of zinc 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate

(Formula I in which A=$-(CH_2-)_2-$; $R_1=R_2=R_3=R_4=CH_3$; $R_5=R_6=H$; R',R''=oxo; B=cyclohexyl; R=$-CO^{\ominus}1/2Zn^{\oplus}$)

381.7 mg (1.115 mmol) of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid described in Example III are suspended in 150 cm³ of double-deionized water, 11.2 cm³ (1.12 mmol) of 0.1 N sodium hydroxide are added and the mixture is stirred in an ultrasonic bath until the contents are dissolved (40 min). 160.4 mg (0.558 mmol) of zinc sulphate $7H_2O$ are then added and the precipitate formed is then drained. After washing with water and drying under vacuum at 70–80°C, 0.41 g of zinc 2-[(5,5,8,8,-tetramethyl-5,6,7,8-tetrahydro-naphthyl)carbonyl]cyclohexanecarboxylate is obtained in the form of a white solid which becomes glassy at approximately 135°C.

EXAMPLES OF FORMULATIONS

Example 1: Antiseborrhoeic lotion

Absolute alcohol	59.0 g
Propylene glycol	40.0 g
2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid	1.0 g

Example 2: Lotion against greasy skin

Absolute alcohol	60.0 g
Polyethylene glycol 400	39.5 g
2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid	0.5 g

In this example for lotion, the active compound may be replaced by 1 g of 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoic acid or by 0.3 g of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid.

Example 3: Lotion for the care of face with a tendency to be affected by acne

Absolute alcohol	42.0 g
Propylene glycol	24.0 g
Purified water	33.0 g
2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2 naphthyl)carbonyl]benzoic acid	1.0 g

The active compound may be replaced by 0.5 g of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid or by 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylic acid.

Example 4: Gel for treatment against greasy skin with a tendency to be affected by acne

Carbopol 941	0.80 g
Absolute alcohol	32.15 g
Propylene glycol	35.00 g
Butylhydroxytoluene	0.02 g
Butylhydroxyanisole	0.03 g
20% Triethanolamine	1.00 g
Purified water	30.0 g
2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid	1.00 g

Example 5: Gel for treatment against greasy skin with a tendency to be affected by acne

Klucel H (cellulose derivative)	1.00 g
Absolute alcohol	70.00 g
Propylene glycol	28.45 g
Butylhydroxytoluene	0.02 g
Butylhydroxyanisole	0.03 g
2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid	0.5 g

The active compound may be replaced by the same quantity of 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoic acid or of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]-cyclohexanecarboxylic acid or by 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylic acid.

Example 6: Cream for greasy skin

Glycol monostearate	4.00 g
Cetyl alcohol	3.50 g
Myrj 53 [polyethylene glycol stearate (50 moles of EO) sold by Atlas]	3.00 g
Capric/caprylic triglyceride	22.00 g
Propyl para-hydroxybenzoate	0.15 g
Butylhydroxytoluene	0.02 g
Butylhydroxyanisole	0.03 g
Propylene glycol	8.00 g
2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid	2.00 g
Water q.s.	100 g

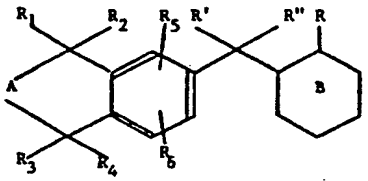
Example 7: (Coloured) stick for applying over restricted areas of skin

Vaseline	19.40 g
Cosbiol (perhydrosqualene)	40.00 g
Solid paraffin	2.00 g
Carnauba was	2.00 g
Ozokerite	9.00 g
Butylhydroxytoluene	0.05 g
Butylhydroxyanisole	0.05 g
Red iron oxide	0.50 g
Yellow iron oxide	1.50 g
Brown iron oxide	2.50 g
Titanium oxide	20.00 g
2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid	1.00 g
Rice starch	2.00 g

The active compound may be replaced by 0.5 g of 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid.

CLAIMS

1. A compound of formula:



(I)

in which:

R_1, R_2, R_3 and R_4 each represent, independently from one another, hydrogen or a lower alkyl radical, with the proviso that at least two of R_1 to R_4 are other than hydrogen;

A represents a methylene or dimethylene radical which may optionally be substituted by a lower alkyl radical with the further possibility that when A represents a dimethylene radical, R_1 and R_3 may together form a methylene or dimethylene radical;

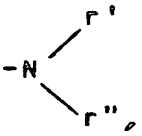
R_5 and R_6 each represents, independently from one another, hydrogen, a halogen, a lower alkyl radical, a lower alkoxy radical, or a hydroxyl radical;

R' represents hydrogen, a hydroxyl radical, a lower alkoxy radical a C_1–C_4 acyloxy radical or an amino radical;

R" represents hydrogen or a lower alkoxy radical, or R' and R" may together form an oxo (=O), methano ($=CH_2$) or hydroxyimino (=N–OH) radical;

B represents a cyclohexyl, cyclohexenyl, cyclohexadienyl or phenyl ring which may be substituted or unsubstituted; and

R represents $-CH_2OH$ or a $-COR_7$ radical, in which R_7 is hydrogen, or an $-OR_4$ radical, or



in which R_8 represents hydrogen, an alkyl radical containing from 1 to 20 carbon atoms, an optionally substituted monohydroxyalkyl, polyhydroxyalkyl, aryl or aralkyl radical or a sugar residue, or r' and r" each represents, independently from one another, hydrogen, a lower alkyl radical, a monohydroxyalkyl radical optionally interrupted by a chain hetero atom, a polyhydroxyalkyl radical, an optionally substituted aryl or benzyl radical, an amino acid or amino sugar residue, or r' and r" may, together with the nitrogen to which they are attached, form a heterocycle; or a salt thereof, including their optical isomers and tautomeric forms, with the exception of 2-[(5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid.

2. A compound according to claim 1 wherein the alkyl radical containing from 1 to 20 carbon atoms is a methyl ethyl, propyl, isopropyl, buty, tert-butyl, 2-ethylhexyl, octyl, dodecyl, hexadecyl or octadecyl radical and the lower alkyl radical is a methyl, ethyl, propyl, isopropyl, butyl or tert-butyl radical.

3. A compound according to claim 1 or 2 wherein the monohydroxyalkyl radical lis a 2-hydroxyethyl, 2-hydroxypropyl or 2-hydroxyethoxyethyl radical.

4. A compound according to any one of claims 1 to 3 wherein the polyhydroxyalkyl radical is a 2,3-dihydroxypropyl or 1,3-dihydroxy-2-propyl radical or a pentaerythritol residue.

5. A compound according to any one of claims 1 to 4 wherein the lower alkoxy radical is a methoxy, isopropoxy, butoxy or tert-butoxy radical.

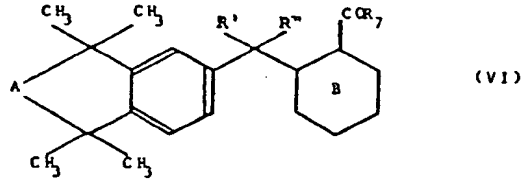
6. A compound according to any one of claims 1 to 5 wherein B is a phenyl ring substituted, in position 3, 4, 5 or 6, by a lower alkyl group, a halogen or an alkoxy group.

7. A compound according to any one of claims 1 to 6 wherein the sugar residue is derived from glucose, mannose, erythrose or galactose.

8. A compound according to any one of claims 1 to 7 wherein the amino sugar residue is derived from glucosamine, galactosamine, mannosamine or meglumine.

9. A compound according to any one of claims 1 to 7 wherein r' and r", together with the nitrogen atom to which they are attached, form a piperidino, piperazino, morpholino, pyrrolidino or 4-(2-hydroxyethyl)-piperazino radical.

10. A compound according to any one of claims 1 to 9 of formula:



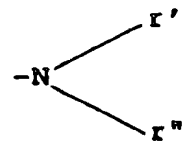
(VI)

in which:

R' and R" together form an oxo radical (=O) or (R' represents a hydroxyl radical and R" represents hydrogen;

A represents a $-(CH_2)_2$ radical or a $-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{CH}}-$ radical;

B represents a phenyl or cyclohexyl ring;

R_7 represents an OR_8 radical or a  radical;

R_8 represents hydrogen or an alkyl radical containing from 1 to 12 carbon atoms;

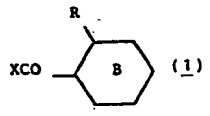
r' represents hydrogen or a monhydroxyalkyl radical,

r" represents an alkyl radical containing from 1 to 8 carbon atoms, a monohydroxyalkyl radical optionally interrupted by a chain hetero atom, or a polyhydroxyalkyl radical,

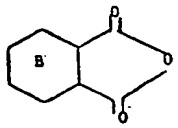
or r' and r", together with the nitrogen to which they are attached, form a 4-(2-hydroxyethyl)-piperazinyl radical; or a salt thereof.

11. A compound according to claim 1 which is:
(1) 2-[(5,5,8,8,-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid,
(2) N-Ethyl-2-[(5,5,8,8,-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(3) Methyl 2-[(5,5,8,8,-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(4) 2'-Ethylhexyl 2-[(5,5,8,8,-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(5) Sodium 2-[(5,5,8,8,-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(6) Zinc 2-[(5,5,8,8,-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(7) 2-[(5,5,8,8,-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzaldehyde,
(8) 2-[(5,5,8,8,-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]phenylcarbinol,
(9) 2-[(5,5,8,8,-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydrooxymethyl]benzoic acid,
(10) N-4'-2-Hydroxyethyl)piperazino-2-[(5,5,8,8,-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(11) 2-[(5,5,8,8,-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)ethoxymethyl]benzoic acid,
(12) 2-[(1,1,2,3,3,-Pentamethyl-5-indanyl)hydroxymethyl]benzoic acid,
(13) 2-[(2-(1,1,2,3,3,-Pentamethyl-5-indanyl)-2-ethenyl]benzoic acid,
(14) 2-[(1,1,2,3,3,-Pentamethyl-5-indanyl)carbonyl]benzoic acid,
(15) N-Ethyl-2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzamide,
(16) Ethyl 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoate,
(17) 2'-Ethylhexyl 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoate,
(18) Sodium 2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzoate,
(19) N-4'-(2-Hydroxyethyl)piperazino-2-[(1,1,2,3,3-pentamethyl-5-indanyl)carbonyl]benzamide,
(20) 2-[(1,1,3,3-Tetramethyl-5-indanyl)hydroxymethyl]benzoic acid,
(21) 2-[(1,1,3,3-Tetramethyl-5-indanyl)carbonyl]benzoic acid,
(22) N-Ethyl-2-[(1,1,3,3-tetramethyl-5-indanyl)carbonyl]benzamide,
(23) N-4'-(2-Hydroxyethyl)piperazino-2-[(1,1,3,3-tetramethyl-5-indanyl)carbonyl]benzamide,
(24) Zinc 2-[(1,1,3,3-tetramethyl-5-indanyl)carbonyl]benzoate,
(25) Ethyl 2-[(5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(26) N-Ethyl-2-[(5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(27) 2-[(5,8-Methano-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzoic acid,
(28) 2-[(1,4-Dimethoxy-5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]benzoic acid,
(29) 2-[(1,4-Dimethoxy-5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoic acid,
(30) N-Ethyl-2-[(1,4,dimethoxy-5,8-methano-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(31) N,N-Di-n-butyl-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(32) 2-[5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylic acid,
(33) 2-[(1,1,2,3,3,-Pentamethyl-5-indanyl)carbonyl]-1-cyclohexene-1-carboxylic acid,
(34) N,N-Di(2-hydroxyethyl)-2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzamide,
(35) Sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate,
(36) 2-[(1,1,2,3,3,-Pentamethyl-5-indanyl)carbonyl]cyclohexanecarboxylic acid,
(37) Ethyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate,
(38) 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylic acid,
(39) Sodium 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)hydroxymethyl]cyclohexanecarboxylate,
(40) Ethyl 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate,
(41) 2-[(5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)methyl]benzoic acid,
(42) Zinc 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]benzoate, or
(43) Zinc 2-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthyl)carbonyl]cyclohexanecarboxylate.

12. A process for the preparation of a compound as defined in any one of claims 1 to 11, which comprises reacting, under the conditions of a Friedel-Crafts reaction, either a substituted acid halide of formula (*1*), or an anhydride of formula (*2*)

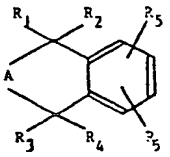


(1)



(2)

with an aromatic compound of formula:



in which A, R_1 to R_6, R and B are as defined in claim 1 and X represents chlorine or bromine, followed by a conventional reaction to prepare other compounds of formula (I) in a known manner if required.

13. A process according to claim 12 wherein the reaction is carried out with an anhydride of formula (2) in the presence of a Lewis acid in a chlorinated solvent.

14. A process according to claim 12 or 13 wherein the keto acid obtained is reduced to the corresponding hydroxy acid by sodium borohydride in tetrahydrofuran or by zinc in an alkali medium.

15. A process according to claim 12 wherein the ketone group of the keto acid obtained is reduced by zinc amalgam in the present of hydrochloric acid.

16. A process according to claim 12 or claim 13 wherein the keto acid is reduced to a diol by lithium aluminium hydride in tetrahydrofuran.

17. A process according to claim 16 wherein the diol is converted into a keto aldehyde by oxidation with pyridinium chlorochromate.

18. A process for preparing a compound of formula (I) as defined in claim 1 substantially as described in any one of Examples I to XXVI.

19. A cosmetic composition which comprises, in a suitable cosmetic vehicle, at least one compound of formula (I) as defined in any one of claims 1 to 11 or as prepared by a process as defined in any one of claims 12 to 18.

20. A cosmetic composition according to claim 19 which comprises from 0.005 to 5% by weight of the compound of formula (I) relative to the total weight of the composition.

21. A cosmetic composition according to claim 20 which comprises from 0.01 to 1% by weight of the compound of formula (I).

22. A compound of formula (I) as defined in any one of claims 1 to 11 for use in a method of treatment of the human or animal body by therapy.

23. A pharmaceutical composition which comprises, in a vehicle suitable for administration by the enteral or the parenteral route, by local application or through the eye, at least one compound of formula (I) as defined in any one of claims 1 to 11 or as prepared by a process as defined in any one of claims 12 to 18.

24. A composition according to claim 23 which is in a form suitable for local application and which comprises from 0.01 to 10% by weight of the compound of formula (I) relative to the total weight of the composition.

25. A composition according to claim 24 which comprises from 0.1 to 5% by weight of the compound of formula (I).

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